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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,117	12/29/2003	Derek O'Hagan	PP020038.0003	1746

27476 7590 09/20/2007

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EXAMINER
MINNIFIELD, NITA M

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
09/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/748,117	O'HAGAN, DEREK	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-85* is/are pending in the application.

4a) Of the above claim(s) *2,8,17 and 29-85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7,9-16 and 18-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5-19-04; 6/20/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed April 16, 2007 is acknowledged and has been entered. Claim 1 has been amended. Claims 1-85 are now pending in the present application.

2. Applicant's election without traverse of Group I, claims 1-28 and species meningitis B and phospholipid in the reply filed on April 16, 2007 is acknowledged. It is noted that claims 1, 3-7, 9-16 and 18-28 read on the elected invention and species; these claims have been examined in the instant application.

3. Claims 2, 8, 17 and 29-85 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and/or species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 16, 2007.

4. The disclosure is objected to because of the following informalities: the titles of the tables in the specification should be at the top of the tables. Appropriate correction is required.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 1, 9, 13-15 and 23-28 are rejected under 35 U.S.C. 102(a) as being anticipated by Haining et al (Blood, 11/16/02, 100/11:Abstract No. 2648) abstract only.

Haining et al discloses an immunogenic composition comprising an antigen, water, polymer microparticles and phospholipids (abstract). Haining et al discloses that the antigen is encapsulated in the microparticle. The prior art anticipates the claimed invention.

Since the Patent Office does not have the facilities for examining and comparing applicant's immunogenic composition with the immunogenic composition of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed immunogenic composition and the immunogenic composition of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

10. Claims 1, 3-7, 9-19 and 22-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Alpar et al (WO 00/56282 publication date 9/28/00).

Alpar et al discloses a pharmaceutical composition which comprises microparticles comprising biologically active compounds capable of generating an immune response, polymeric material capable of forming microspheres and an immunostimulant comprising a phospholipid (abstract; claims; page 3, lines 30-35). Alpar et al discloses that the presence of phospholipids in a vaccine formulation has an immunostimulant effect (page 3, lines 6-7). Alpar et al also discloses that immunostimulants are adjuvants (Freunds, alhydrogel, aluminium

compounds) (p. 3; p. 7). The prior art discloses that a microencapsulated biologically active formulation, especially of immunogens, which comprises a phospholipids in addition to the polymeric material used in the formation of the microparticles, has an increased biological effect (page 3, lines 21-25). Alpar et al discloses that the microparticles, also called microcapsules or microspheres, are made of polymeric materials such as poly (hydroxy) acid, poly-(L-lactide), poly(lactic/glycolic acid), polycyonacrylates, polyanhydrides and polycaprolactones (page 5, lines 1-7). Alpar et al discloses various phospholipids (page 5, lines 9-19). Alpar et al discloses that the antigen can be a polynucleotide-containing antigen (pp. 5-6). Alpar et al discloses intramuscular (i.m.) injection of the composition (p. 4). Aplar et al discloses the claimed range of microparticle diameter size (p. 5, l. 28-29). Alpar et al discloses that the antigen can be encapsulated and that the phospholipids can be distributed (i.e. entrapped or adsorbed) throughout the microparticle (p. 8). Alpar et al discloses that the composition can comprise pharmaceutically acceptable carriers (solid or liquid) (p. 8). The prior art anticipates the claimed invention.

Since the Patent Office does not have the facilities for examining and comparing applicant's immunogenic composition with the immunogenic composition of the prior art reference, the burden is upon applicants to show a distinction between the material structural and functional characteristics of the claimed immunogenic composition and the immunogenic composition of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

11. Claims 1, 3-7, 9-16 and 18-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alpar et al (WO 00/56282 publication date 9/28/00) in view of Muttilainen (Microbial Pathogenesis, 1995, 18:423-436) and Cox et al (Vaccine, 1997, 15/3:248-256).

Alpar et al teaches a pharmaceutical composition which comprises microparticles comprising biologically active compounds capable of generating an immune response, polymeric material capable of forming microspheres and an immunostimulant comprising a phospholipid (abstract; claims; page 3, lines 30-35). Alpar et al teaches that the presence of phospholipids in a vaccine formulation has an immunostimulant effect (page 3, lines 6-7). Alpar et al also teaches that immunostimulants are adjuvants (Freunds, alhydrogel, aluminium compounds) (p. 3; p. 7). The prior art teaches that a microencapsulated biologically active formulation, especially of immunogens, which comprises a phospholipids in addition to the polymeric material used in the formation of the microparticles, has an increased biological effect (page 3, lines 21-25). Alpar et al teaches that the microparticles, also called microcapsules or microspheres, are made of polymeric materials such as poly (hydroxy) acid, poly-(L-lactide), poly(lactic/glycolic acid), polycyonacrylates, polyanhydrides and polycaprolactones (page 5, lines 1-7). Alpar et al teaches various phospholipids (page 5, lines 9-19). Alpar et al teaches that the antigen can be a polynucleotide-containing antigen (pp. 5-6). Alpar et al teaches intramuscular (i.m.) injection of the composition (p. 4). Aplar et al teaches the claimed range of microparticle diameter size (p. 5, l. 28-29). Alpar et al teaches that the antigen can be encapsulated and that the phospholipids can be distributed (i.e. entrapped or adsorbed) throughout the microparticle (p. 8). Alpar et al teaches that the composition can comprise pharmaceutically acceptable

carriers (solid or liquid) (p. 8). The prior art teaches the claimed invention except for the antigen being derived from a pathogenic organism (bacterium, meningitis B).

However, Muttilainen et al teaches a composition comprising meningitis B antigen, the P1 protein, in a phospholipid vesicles or liposomes (abstract, methods and materials). Muttilainen et al teaches the liposome formulation (P1 protein and liposomes) is good as an adjuvant (p. 432).

Cox et al teaches that the "purpose of adjuvant combinations is to combine various adjuvant components to achieve the desired mix of immunological responses. The best-known adjuvant combination is Freund's complete adjuvant (FCA) which combines the immunomodulatory properties of ***Mycobacterium tuberculosis*** (essentially TDM and MDP) along with the short-term depot effect of w/o emulsions, This adjuvant generates very strong Thl and Th2 responses and is especially suited to hydrophilic immunogens. The Ciba-Geigy adjuvant formulation is a modification of FCA which uses a metabolizable oil (squalene) and nor-MDP. It has been used successfully in clinical trial. Despite the success of w/o formulations as a basis for adjuvant combinations (especially FCA and TiterMax) they do not normally induce CTL responses and require multiple doses for effective immunization i.e. long-term depots are not established." (p. 253)

Cox et al teaches that "[L]iposomes offer a versatile formulation into which various immunomodulatory molecules can be incorporated. Examples include MPL, lipophilic MDP and Quil A. Although hydrophilic molecules can be incorporated within a liposome, the efficiency is generally low and liposome formulations are most suited for amphipathic immunogens. One other interesting combination is the mixture of MPL and QS21. Selection of the "best" adjuvant

combination requires some knowledge of the chemical nature of the protective immunogen(s) and some idea of the nature of the immune response which is likely to be protective. However, even where knowledge of both these issues is minimal, rational selection of a small number of basic formulations and additives should permit selection of an effective adjuvant system. It is hoped that this review will help in this rational selection." (p. 253)

Barring any unexpected results and/or convincing evidence to the contrary, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the teachings of Alpar et al, Muttilainen et al and Cox et al with a reasonable expectation of success to prepare the immunogenic composition as instantly claimed. Cox et al teaches that using a combination of adjuvants is desirable to achieve a mix of immunological responses.

12. No claims are allowed.

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM

September 16, 2007